Alcon

[redacted] **Protocol for CLL949-E003**

Title: Clinical Characterization of an Investigational Frequent Replacement Daily Wear Silicone Hydrogel Sphere Contact Lens

Protocol Number:	CLL949-E003 / NCT04702984
Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	LID021201

Investigator Agreement:

- I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, all applicable regulatory authority regulations, and conditions of approval imposed by the reviewing IRB or regulatory authority.
- I will supervise all testing of the device involving human subjects and ensure that the requirements relating to obtaining informed consent and IRB review and approval are met in accordance with applicable local and governmental regulations.
- I have read and understand the appropriate use of the investigational product(s) as described in the protocol, current Investigator's Brochure, product information, or other sources provided by the Sponsor.
- I understand the potential risks and side effects of the investigational product(s).
- I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.
- I agree to comply with all other requirements regarding the obligations of clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

Have you ever been disqualified as an Investigator by any Regulatory Authority? ☐ No ☐Yes
Have you ever been involved in a study or other research that was terminated? ☐ No ☐Yes If yes, please explain here:

Principal Investigator:

Signature Date

Name and professional position:

Address:

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon Research, LLC 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	LID021201
Name of Control Product(s)	N/A
Title of Trial	Clinical Characterization of an Investigational Frequent Replacement Daily Wear Silicone Hydrogel Sphere Contact Lens
Protocol Number	CLL949-E003
Number of Sites Country	~3 US
Planned Duration of Exposure	Test Product: ~ 7 days
Number of Subjects	Target to complete: 30
	Planned to enroll: ~ 48
Study Population	Volunteer subjects aged 18 or over who are habitual spherical daily wear soft frequent replacement contact lens wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week for at least 8 hours per day.
Objective(s)	The primary objective of this study is to evaluate the clinical performance of an investigational frequent replacement daily wear silicone hydrogel (SiHy) sphere contact lens [redacted] over 7 days of daily wear. [redacted]
Endpoints	Primary Effectiveness • Front surface wettability [redacted]

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness [redacted]

<table>
<tr><td></td><td colspan="2">[redacted]
• Lens surface evaluation (front surface wettability, [redacted]
[redacted]
Safety
• AEs
• Biomicroscopy
• Device deficiencies</td></tr>
<tr><td rowspan="3">Study Design</td><td>☒ Prospective</td><td>☐ Single-masked (trial subject)</td></tr>
<tr><td>☒ Single group
☐ Parallel group
☐ Crossover
☐ Other</td><td>☐ Single-masked (Investigator)
☐ Double-masked
☒ Open-label
☐ Other</td></tr>
<tr><td>☐ Contralateral
☒ Bilateral
☐ Monocular lens wear</td><td>☐ Randomized</td></tr>
<tr><td rowspan="3">Test Product Details</td><td>[redacted]</td><td>[redacted]</td></tr>
<tr><td>LID Number</td><td>LID021201</td></tr>
<tr><td>Manufacturer</td><td>Alcon Laboratories, Inc.
6201 South Freeway</td></tr>
</table>

		Fort Worth, Texas 76134-2099 USA
	[redacted]	[redacted]
	[redacted]	[redacted]
Inclusion Criteria	1. Subject must be at least 18 years of age. 2. Subject must be able to understand and must sign an ICF that has been approved by an IRB. 3. Successful wear of spherical daily wear frequent replacement soft contact lenses in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months. [redacted] 8. Subject must be willing to stop wearing their habitual contact lenses for the duration of study participation. [redacted].	
Exclusion Criteria	1. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator. 2. Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator. 3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye.	

	[redacted] 6. Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear. [redacted] 10. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment. [redacted]
Associated Materials	• OPTI-FREE® RepleniSH® multipurpose solution (OFR) for contact lens cleaning and disinfecting will be used with the study lenses • [redacted].

Table 1-1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Order Spectacles	Visit 2† Dispense	Visit 3 Week 1 Follow-up/ Exit	Early Exit	USV
		[redacted]	[redacted]		
Informed Consent	✓	-	-	-	-
Demographics	✓	-	-	-	-
Medical History*	✓	✓**	✓	✓	✓
Concomitant Medications*	✓	✓**	✓	✓	✓
Inclusion/Exclusion	✓	-	-	-	-
Habitual lens (brand, power* and lenscare)	✓	-	-	-	-
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Biomicroscopy	✓	✓**	✓	✓	✓
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Dispense study lenses*∞	-	✓	-	-	-
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Order Spectacles	Visit 2† Dispense	Visit 3 Week 1 Follow-up/ Exit	Early Exit	USV
[redacted]		[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lens surface assessments (OD, OS): • Front surface wettability [redacted]	-	✓	✓	✓	(✓)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	Visit 1 Screening/ Baseline/ Order Spectacles	Visit 2† Dispense	Visit 3 Week 1 Follow-up/ Exit	Early Exit	USV
		Day 1 (+ 0 to 4 Days after V1)	7-1 days from dispense[$]		
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
AEs[Ω]	✓	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓	✓
Exit Form	(✓)	(✓)	✓	(✓)	(✓)

[redacted]

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
[redacted]	[redacted]
CFR	Code of Federal Regulations
[redacted]	[redacted]
D/C	Discontinue
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed consent form
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LID	Lens identification
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
N/A	Not applicable
OD	Right eye
OFR	OPTI-FREE RepleniSH multipurpose solution
OS	Left eye
OU	Both eyes
SAE	Serious adverse event
SADE	Serious adverse device effect
SiHy	Silicone hydrogel
US	United States
USV	Unscheduled visit
VA	Visual acuity

2 TABLE OF CONTENTS

[redacted]

List of Tables

List of Figures

3 INTRODUCTION

3.1 Study Rationale and Purpose

[redacted]

The purpose of this study is to obtain on-eye performance data of the investigational lenses [redacted]

[redacted]

3.2 Trial Objective

The primary objective of this study is to evaluate the clinical performance of an investigational frequent replacement daily wear silicone hydrogel (SiHy) sphere contact lens, [redacted], over 7 days of daily wear.

3.3 Risks and Benefits

[redacted] Material properties and design characteristics of the contact lens [redacted] are features consistent with successful contact lens wear.

[redacted]

[redacted]

The site personnel will educate subjects on proper hygiene and lens handling, and compliance with the use of contact lenses according to the protocol. Subjects should be instructed not to wear contact lenses while sleeping or swimming. The site personnel will also advise the subjects to remove contact lenses and return for prompt follow-up of symptoms, such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

3.4 Subject Population

The study population includes approximately 48 volunteer subjects to be enrolled at approximately 3 sites, with approximately 16 subjects enrolled per site. The study population will consist of subjects with normal eyes (other than the need for optical correction for refractive ametropia), who are adapted, existing wearers of soft frequent replacement daily wear contact lenses in both eyes,

[redacted]

3.5 Outline of Study

This will be a multi-site, prospective, single arm, open-label study examining 1 type of contact lens. The expected duration of subject participation in the study is approximately 7 days, with up to 3 scheduled visits. The study is expected to be completed in approximately 6 weeks.

4 TREATMENTS ADMINISTERED

All subjects will receive the test lens to wear bilaterally throughout the study duration.

4.1 Identity of Study Treatments

	Test Lens
LID Number	LID021201
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

	[redacted]
Usage	• Wear: ○ Daily Wear ○ Bilateral ○ Single arm open-label [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5 STUDY PROCEDURES AND ASSESSMENTS

5.1 Visits and Examinations

5.1.1 Visit 1 – Screening/Baseline/Order Spectacles

1	Explain the purpose and nature of the study, and have the subject read, sign, and date the IRB-approved informed consent document. [redacted]
2	Obtain demographic information and medical history, including information on all medications used within the past 30 days. [redacted]
3	[redacted] Record habitual lens information (brand, power) and lens care information (brand). *If subject is wearing contact lenses, ask them to remove them after taking VA.*
[redacted]	[redacted]
[redacted]	[redacted]

6	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: [redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
11	Assess and record any device deficiencies and AEs reported or observed during the study visit. • *Note: AEs must be recorded for all enrolled subjects from the time of signature of informed consent including those subjects who screen fail.*
[redacted]	[redacted]
13	Schedule Visit 2 [redacted]

5.1.2 Visit 2 [redacted] – Dispense Study Lens

[redacted]	[redacted].
2	Assess and record any device deficiencies and AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit(s).

[redacted]	[redacted]
4	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: [redacted] • Other findings
5	Have the subject insert the appropriate study lenses, being careful to maintain the correct OD and OS lens assignments [redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
10	Evaluate the study lenses by performing the following assessments*: [redacted] • Lens surface evaluation (front surface wettability, [redacted] [redacted]
[redacted]	[redacted]
12	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those that screen fail, as applicable.*
[redacted]	[redacted]
14	Schedule Visit 3 [redacted] [redacted] [redacted] [redacted]
15	[redacted]

5.1.3 Visit 3 [redacted] – Week 1 Follow-up/Exit

[redacted]	[redacted]
2	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted] [redacted]
[redacted]	[redacted] [redacted]
[redacted]	[redacted] [redacted] [redacted]
9	Evaluate the study lenses by performing the following assessments*: • [redacted] • Lens surface evaluation (front surface wettability, [redacted] [redacted]

[redacted]	[redacted]
11	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: [redacted]
[redacted]	[redacted]
[redacted]	[redacted] [redacted]s [redacted]
14	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those subjects who screen fail, as applicable.*
15	Exit the subject from the study.

5.2 Unscheduled Visits

[redacted]

- Collect AE and Device Deficiency information
- [redacted]
- [redacted]

- Perform biomicroscopy (assessments with or without lenses, as possible)

[redacted]

5.3 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after signing the informed consent, including screen failures. Subjects may discontinue from the study at any time for any reason. [redacted]

5.4 Clinical Study Termination

The Study Sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time, for reasonable cause.

[redacted]

[redacted]

6 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with frequencies and percentages from each category.

[redacted]

6.1 Subject Evaluability

The final subject evaluability will be determined prior to locking the database, based on the Deviations and Evaluability Plan.

6.2 Analysis Data Sets

6.2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis.

[redacted]

For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed.

6.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the Safety Analysis Set. [redacted]

6.4.1 Primary Effectiveness

The primary objective of this study is to evaluate the clinical performance of an investigational frequent replacement daily wear SiHy sphere contact lens. [redacted], over 7 days of daily wear. The primary endpoint is front surface wettability, collected on a 5-point scale, for each eye.

6.4.1.1 Statistical Hypotheses

No inferences are to be made on the primary effectiveness endpoint; therefore, no hypotheses are formulated.

6.4.1.2 Analysis Methods

Descriptive statistics will be presented, to include frequencies and percentages in each grade [redacted]

[redacted]

[redacted]

[redacted]

6.6 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out.

[redacted]

6.8 Safety Analysis

The safety endpoints for this study are AEs, biomicroscopy findings, and device deficiencies.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. [redacted]

No inferential testing will be done for safety analysis.

[redacted]

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

Terms and Definitions

Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (test product). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.*
Adverse Device Effect (ADE)	AE related to the use of an investigational medical device (test *product*) or control *product*. *Note: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test product or control product.*
Anticipated Serious Adverse Device Effect (ASADE)	Serious ADE which by its nature, incidence, severity or outcome has been identified in the risk management file.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.*
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended

	performance of the device refers to the intended use for which the device is labeled or marketed.
Nonserious Adverse Event	AE that does not meet the criteria for an SAE.
Serious Adverse Event (SAE)	AE that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in: a) a life-threatening illness or injury. *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* b) any potentially sight-threatening event or permanent impairment to a body structure or a body function. c) in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered an SAE. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.* d) a medical or surgical intervention to prevent a) or b). e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect. *Refer to Section 7.1 for additional SAEs.*

Serious Adverse Device Effect (SADE)	ADE that has resulted in any of the consequences characteristic of an SAE.
Significant Nonserious Adverse Event	A significant nonserious AE is a symptomatic, device-related, nonsight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 7.1 for additional Significant Nonserious AEs.*
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk management file.
Use Error	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.*

7.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test *product*).

Figure 7–1 Categorization of All AEs

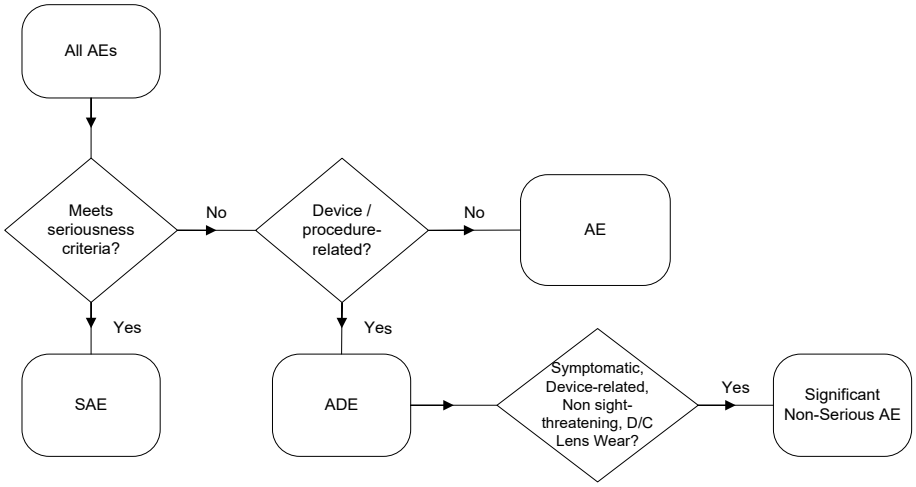
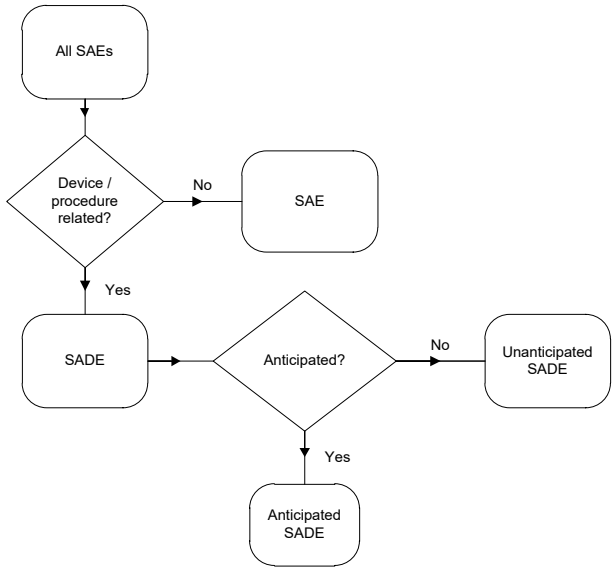


Figure 7-2 Categorization of All Serious Adverse Events



[redacted]

[redacted]

[redacted]

- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- [redacted]
- [redacted]

[redacted]

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. [redacted]

[redacted]

[redacted]

7.2 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take since your last study visit?"

[redacted]

7.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any pre-existing medical conditions or signs/symptoms present in a subject prior to the start of the study (ie, before informed consent is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

[redacted]

[redacted]

[redacted]

[redacted]

7.5 Follow-Up of Subjects with Adverse Events

The Investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

7.6 Pregnancy in the Clinical Study

Women of childbearing potential or women who are pregnant at the time of study entry are not excluded from participation.

8 CONFIDENTIALITY, BIAS, AND MASKING

8.1 Subject Confidentiality and Methods Used to Minimize Bias

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study.

This is an open label study with all subjects assigned to wear LID021201 bilaterally for the duration of the 1-week treatment period.

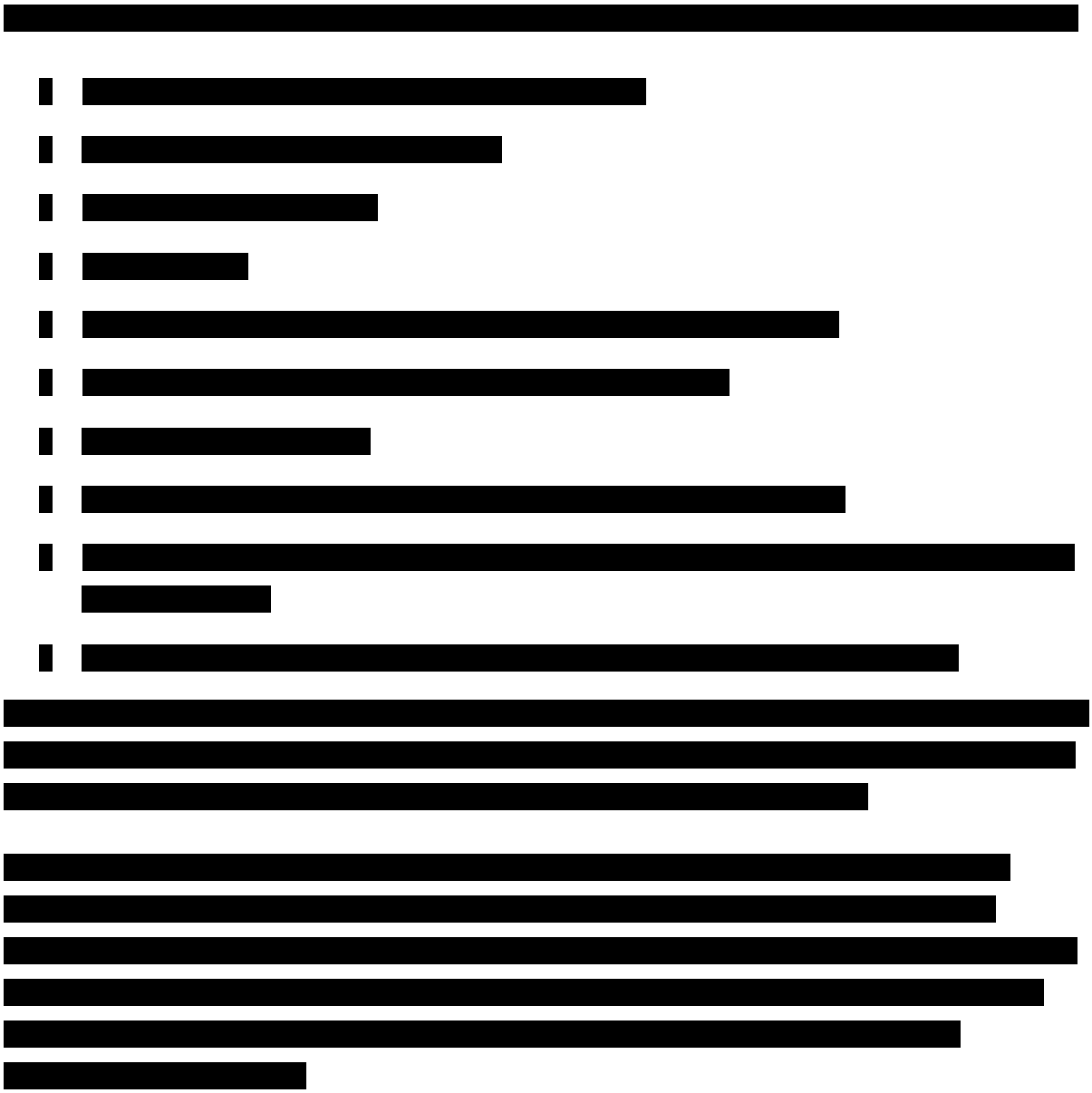
8.2 Unmasking of the Study Treatment

Not applicable; this study is open-label.

9 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

9.1 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the eCRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Study monitors are appointed by the Study Sponsor and are independent of study site staff. If electronic records are maintained, the method of verification must be determined in advance of starting the study.



[redacted]

9.3 Regulatory Documentation and Records Retention

The Investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the Sponsor and the Investigator's files will be reviewed as part of the ongoing study monitoring. [redacted]

[redacted]

10 ETHICS AND COMPLIANCE

This trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the referenced directives, regulations, guidelines, and/or standards.

10.1 Compliance

The Investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The Investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. [redacted]

10.2 Institutional Review Board (IRB)

This trial requires IRB approval prior to initiation. This protocol, subject informed consent, and subsequent amendments will be reviewed and approved by an IRB.

[redacted]